

What is claimed is:

1. A non-chemokine agent capable of binding to a chemokine receptor and inhibiting fusion of HIV-1 to CD4<sup>+</sup> cells with the proviso that the agent is not a known bicyclam or its known derivative.
2. The non-chemokine agent of claim 1, wherein the non-chemokine agent is a oligopeptide.
3. The non-chemokine agent of claim 1, wherein the non-chemokine agent is a nonpeptidyl agent.
4. The non-chemokine agent of claim 1, wherein the non-chemokine agent is a polypeptide.
5. The non-chemokine agent of claim 4, wherein the polypeptide is an antibody or a portion of an antibody.
6. The non-chemokine agent of claim 4, wherein the polypeptide comprises amino acid sequence as set forth in SEQ ID NO 5.
7. The non-chemokine agent of claim 4, wherein the polypeptide comprises the MIP-1 $\beta$  sequence with the deletion of the first seven N-terminal amino acids of said sequence.
8. The non-chemokine agent of claim 4, wherein the polypeptide comprises the MIP-1 $\beta$  sequence with the deletion of the first eight N-terminal amino acids of said sequence.
9. The non-chemokine agent of claim 4, wherein the polypeptide comprises the MIP-1 $\beta$  sequence with the deletion of the first nine N-terminal amino acids of said sequence.

10. The non-chemokine agent of claim 4, wherein the polypeptide comprises the MIP-1 $\beta$  sequence with the deletion of the first ten N-terminal amino acids of said sequence.
11. The non-chemokine agent of claim 4, wherein the polypeptide comprises the MIP-1 $\beta$  sequence with the N-terminal sequence modified by addition of an amino acid or oligopeptide.
12. The non-chemokine agent of claim 4, wherein the polypeptide comprises the MIP-1 $\beta$  sequence with the N-terminal sequence modified by removing the N-terminal alanine and replacing it by serine or threonine and an additional amino acid or oligopeptide or nonpeptidyl moiety.
13. The non-chemokine agent of claim 11 or 12, wherein the additional amino acid is methionine.
14. An non-chemokine agent capable of binding to CXCR4 and inhibiting HIV-1 infection with the proviso that the agent is not a known bicyclam or its known derivative.
15. The non-chemokine agent of claim 14, wherein the agent is an oligopeptide.
16. The non-chemokine agent of claim 14, wherein the agent is a polypeptide.
17. The non-chemokine agent of claim 16, wherein the polypeptide comprises the SDF-1 sequence with the deletion of the first six N-terminal amino acids of said sequence.
18. The non-chemokine agent of claim 16, wherein the polypeptide comprises the SDF-1 sequence with the

deletion of the first seven N-terminal amino acids of said sequence.

- 5 19. The non-chemokine agent of claim 16, wherein the polypeptide comprises the SDF-1 sequence with the deletion of the first eight N-terminal amino acids of said sequence.
- 10 20. The non-chemokine agent of claim 16, wherein the polypeptide comprises the SDF-1 sequence with the deletion of the first nine N-terminal amino acids of said sequence.
- 15 21. The non-chemokine agent of claim 16, wherein the N-terminal glycine of SDF-1 is replaced by serine and derivatized with biotin.
- 20 22. The non-chemokine agent of claim 16, wherein the N-terminal glycine of SDF-1 is replaced by serine and derivatized with methionine.
- 25 23. The non-chemokine agent of claim 16, wherein the N-terminus of SDF-1 is modified by the addition of a methionine before the terminal glycine.
- 30 24. The agent of claim 16, wherein the agent is an antibody or a portion of an antibody.
- 35 25. The agent of claim 14, wherein the agent is a non-peptidyl agent.
26. A pharmaceutical composition comprising an amount of the non-chemokine agent of claim 1 effective to inhibit fusion of HIV-1 to CD4<sup>+</sup> cells and a pharmaceutically acceptable carrier.
27. A pharmaceutical composition comprising an amount of the non-chemokine agent of claim 14 effective to

inhibit fusion of HIV-1 to CD4<sup>+</sup> cells and a pharmaceutically acceptable carrier.

- 5 28. A composition of matter capable of binding to a chemokine receptor and inhibiting fusion of HIV-1 to CD4<sup>+</sup> cells comprising a non-chemokine agent linked to a ligand capable of binding to a cell surface receptor of the CD4<sup>+</sup> cells other than the chemokine receptor such that the binding of the non-chemokine agent to the chemokine receptor does not inhibit the binding of the ligand to the other receptor.
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- 15 29. The composition of matter of claim 28, wherein the cell surface receptor is CD4.
30. The composition of matter of claim 28, wherein the ligand comprises an antibody or a portion of an antibody.
- 20 31. A pharmaceutical composition comprising an amount of the composition of matter of claim 28 effective to inhibit fusion of HIV-1 to CD4<sup>+</sup> cells and a pharmaceutically acceptable carrier.
- 25 32. A method for reducing the likelihood of HIV-1 infection in a subject comprising administering the pharmaceutical composition of claim 26, 27, or 31 to the subject.
- 30 33. A method for treating HIV-1 infection in a subject comprising administering the pharmaceutical composition of claim 26 or 27 to the subject.
- 35 34. A method for determining whether an agent is capable of inhibiting HIV-1 infection comprising steps of:
- (a) contacting an appropriate concentration of an agent with a chemokine receptor or a portion

contacting the chemokine receptor resulting from step (a) with a gp120/CD4 complex under conditions permitting the binding of the gp120/CD4 complex and the chemokine receptor in the absence of the agent;

(b) contacting the chemokine receptor resulting from step (a) with a gp120/CD4 complex under conditions permitting the binding of the gp120/CD4 complex and the chemokine receptor in the absence of the agent;

(c) measuring the amount of bound gp120/CD4 complex wherein a decrease in the amount compared with the amount determined in the absence of the agent indicates that the agent is capable of inhibiting HIV-1 infection.

35. A method for determining whether an agent is capable of inhibiting HIV-1 infection comprising steps of:

(a) fixing a chemokine receptor on a solid matrix;

(b) contacting the agent with the fixed chemokine receptor under conditions permitting the binding of the agent to the chemokine receptor;

(c) removing the unbound agent;

(d) contacting the fixed chemokine receptor resulting in step (c) with a gp120 in the presence of CD4 under conditions permitting the binding of the gp120/CD4 complex and the chemokine receptor in the absence of the agent;

(e) measuring the amount of bound gp120/CD4 complex; and

(f) comparing the amount determined in step (d) with the amount determined in the absence of the agent, a decrease of the amount indicating

that the agent is capable of inhibiting HIV-1 infection.

36. A method for determining whether an agent is capable of inhibiting HIV-1 infection comprising steps of:

- (a) fixing a chemokine receptor on a solid matrix;
- (b) contacting the agent with the fixed chemokine receptor;
- (c) contacting the mixture in step (b) with a gp120 in the presence of CD4 under conditions permitting the binding of the gp120/CD4 complex and the chemokine receptor in the absence of the agent;
- (d) measuring the amount of bound gp120/CD4 complex; and
- (e) comparing the amount determined in step (d) with the amount determined in the absence of the agent, a decrease of the amount indicating that the agent is capable of inhibiting HIV-1 infection.

37. A method for determining whether an agent is capable of inhibiting HIV-1 infection comprising steps of:

- (a) contacting the agent with a gp120/CD4 complex under conditions permitting the binding of the agent to the gp120/CD4 complex;
- (b) contacting the gp120/CD4 complex resulting from step (a) with a chemokine receptor under conditions permitting the binding of the gp120/CD4 complex and the chemokine receptor in the absence of the agent;

(c) measuring the amount of bound chemokine receptor, wherein a decrease of the amount when compared with the amount determined in the absence of the agent indicates that the agent is capable of inhibiting HIV-1 infection.

38. A method for determining whether an agent is capable of inhibiting HIV-1 infection comprising steps of:

- (a) fixing a gp120/CD4 complex on a solid matrix
- (b) contacting the agent with the fixed gp120/CD4 complex under conditions permitting the binding of the agent to the gp120/CD4 complex;
- (c) removing unbound agent;
- (d) contacting the fixed gp120/CD4 complex resulting from step (c) with a chemokine receptor under conditions permitting the binding of the gp120/CD4 complex and the chemokine receptor in the absence of the agent;
- (e) measuring the amount of bound chemokine receptor; and
- (f) comparing the amount determined in step (e) with the amount determined in the absence of the agent, a decrease of the amount indicating that the agent is capable of inhibiting HIV-1 infection.

39. A method for determining whether an agent is capable of inhibiting HIV-1 infection comprising steps of:

- (a) fixing a gp120/CD4 complex on a solid matrix;

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- (b) contacting the agent with the fixed gp120/CD4 complex;
- (c) contacting the mixture in step (b) with a chemokine receptor under conditions permitting the binding of the gp120/CD4 complex and the chemokine receptor in the absence of the agent;
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- (d) measuring the amount of bound chemokine receptor; and
- (e) comparing the amount determined in step (d) with the amount determined in the absence of the agent, a decrease of the amount indicating that the agent is capable of inhibiting HIV-1 infection.
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40. The method of claim 34, 35, 36, 37, 38 or 39 wherein the CD4 is a soluble CD4.
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41. The method of claim 34, 35, 36, 37, 38 or 39 wherein the chemokine receptor is CCR5.
42. The method of claim 34, 35, 36, 37, 38 or 39 wherein the chemokine receptor is CXCR4.
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43. The method of claim 34, 35, 36, 37, 38 or 39 wherein the chemokine receptor is expressed on a cell.
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44. The method of claim 43, wherein the chemokine receptor is embedded in liposomes.
45. The method of claim 43, wherein the chemokine receptor is embedded in a membrane derived from cells expressing the chemokine receptor.
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46. The method of claim 43, wherein the cell is a L1.2 cell.



47. The method of claim 35 or 36, wherein the gp120, CD4 or both are labelled with a detectable marker.
48. The method of claim 37, 38 or 39, wherein the chemokine receptor is labelled with a detectable marker.
49. The method of claim 47 or 48, wherein the gp120, CD4 or the chemokine receptor is labelled with biotin.
50. The method of claim 49, wherein the biotinylated gp120, CD4 or the chemokine receptor is detected by:
- (i) incubating with streptavidin-phycoerythrin,
  - (ii) washing the incubated mixture resulting from step (i), and
  - (iii) measuring the amount of bound gp120, CD4 or the chemokine receptor using a fluorometer, exciting at 530nm and reading the emission at 590nm.
51. The agent determined to be capable of inhibiting HIV-1 infection by the method of claim 34, 35, 36, 37, 38 or 39 which is previously unknown.
52. A pharmaceutical composition comprising the agent determined to be capable of inhibiting HIV-1 infection by the method of claim 34, 35, 36, 37, 38 or 39 and a pharmaceutically acceptable carrier.
53. The method of claim 34, 35, 36, 37, 38 or 39 wherein the agent is an oligopeptide.
54. The method of claim 34, 35, 36, 37, 38 or 39 wherein the agent is a polypeptide.

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